





A method of protein engineering including the steps of:-

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- creating a computer database which includes a (i) plurality of entries, each said entry corresponding to a description of a location and orientation in 3D space of side chains of amino acid residues of a framework protein, wherein the location and orientation of each side chain is simplified as a  $\not C\alpha$ -C $\beta$  vector;
- creating a query corresponding to a description of a (ii) location and orientation/in 3D space of respective side chains of two or more/amino acid residues of a sample protein which are required for a function of said sample protein, wherein the location and orientation of each side chain is simplified as a  $C\alpha$ -C $\beta$  vector; and
- searching said database with said query to thereby (iii) identify one or more hits wherein at least one of said hits corresponds to a respective said framework protein which has structural similarity to said sample protein.

A method of protein engineering including the steps of:-20 2.

- creating a computer database which includes a (i) plurality of entries, each said entry corresponding to a description of a location and orientation in 3D space of amino acid residues of a framework protein capable of internal disulfide bond/formation;
- creating a query corresponding to a description of a (ii) location and orientation in 3D space of two or more amino acid residues of a sample protein which are required for a function of said sample protein; and
- (iii) searching said database with said query to thereby identify one or more hits wherein at least one of said

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hits corresponds to a respective said framework protein which has structural similarity to said sample protein.

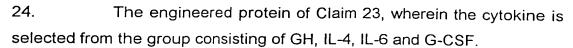
- 3. The method of Claim 1, wherein the framework protein is capable of internal disulfide bond formation.
  - 4. The method of Claim 3, wherein said framework protein is a small cysteine rich protein which comprises 70 amino acids or less, having 2-11 disulfide bonds.
- 5. The method of Claim 2, wherein said framework protein is a small cysteine rich protein which comprises 70 amino acids or less, having 2-11 disulfide bonds.
- 6. The method of 5, wherein the location and orientation of a side-chain of each said amino acid residue of said framework protein and the location and orientation of a side-chain of each of said two or more amino acid residues of said sample protein is simplified as a respective Cα-Cβ vector.
  - 7. The method of any one of Claims 1, 3, 4 or 6, wherein the  $C\alpha$ - $C\beta$  vector is in the form of a distance matrix representation.
  - 8. The method of Claim 1 or Claim 2, further including the step of modifying an amino acid sequence of said framework protein which corresponds to a hit, by substituting at least one amino acid residue thereof with at least one amino acid residue of said sample protein to thereby create a modified framework protein.
  - The method of Claim 8, wherein the at least one amino acid residue of said sample protein represents at least a portion of at least one functional region of said sample protein.
    - 10. The method of Claim 9, wherein at least two of the amino acid residues of said sample protein which substitute amino acid residues of said framework protein are non-contiguous in primary sequence.
- 30 11. The method of any one of Claims 8-10, wherein the modified framework protein has greater stability than said sample protein.

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- 12. The method of any one of Claims 8-11, wherein the modified framework protein has increased structural similarity to said sample protein.
- 13. The method of Claim 12, wherein the modified framework protein is capable of exhibiting a function which is either similar to, or inhibitory of, a function of said sample protein.
- 14. The method of any preceding claim, wherein the sample protein is a cytokine.
  - 15. The method of Claim 14, wherein the cytokine is selected 10 from the group consisting of GH, IL-4, IL-6 and G-CSF.
- 16. The method of Claim 1/or Claim 2, wherein at step (iii) the hits are ranked according to structural similarity with said sample protein.
  - The method of Claim 1 or Claim 2, wherein searching at step (iii) includes:
    - (a) identification of said hits by clique detection;
    - (b) filtering of said hits identified at step (a).
    - 18. A modified framework protein produced according to the method of any one of Claims 9-15.
    - 19. The modified framework protein of Claim 18, which protein is 20 a cytokine mimetic.
    - 20. An engineered protein comprising 70 amino acid residues or less of a framework protein and 2-11 disulfide bonds of said framework protein, together with at least two amino acid residues of another protein which are non-contiguous in primary sequence and represent at least a portion of a functional region of said another protein.
      - 21. The engineered protein of Claim 20, which protein has greater stability than said another protein.
      - 22. The engineered protein of Claim 21, which protein exhibits a function either similar to, or inhibitory of, said another protein.
- 30 23. The engineered protein of any one of Claims 20-22, wherein said another protein is a cytokine.

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- 25. The engineered protein of Claim 24, said engineered protein having an amino acid sequence selected from the group consisting of SCY01, SCY02, SCY03, ERP01, ERP02, ERP03 and VIBO1.
  - 26. The engineered protein of Claim 25, which protein is a cytokine mimetic.
- A computer program for searching a protein database which comprises a plurality of entries, each said entry corresponding to a
  distance matrix representation of two or more Cα-Cβ vectors, said program including the steps of:
  - (i) comparing a query with each said database entry, said query corresponding to a distance matrix representation of two or more Cα-Cβ vectors; and
- (ii) identifying hits by clique detection, wherein a hit is defined according to a minumum number of Cα-Cβ vector matches between said query and each said entry.
- 28. A computer program which filters said hits identified at step 20 (ii) of Claim 27.
  - 29. A computer program according to Claim 27, which program is a VECTRIX program as described herein.
  - 30. A computer program according to Claim 28, which program is a POSTVEC program as described herein.

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